REMARKS

I. Claim Status

Claims 3-8 are currently pending and stand rejected. No claims are amended herein.

II. Obviousness Rejection

The Office rejected claims 3-8 under 35 U.S.C. § 103(a) as unpatentable over U.S. Patent Application Publication No. 2001/0041729 to Paralkar et al. ("Paralkar") in view of Pagel, P. S., et al. "Pharmacology of Levosimendan: A New Myofilament Calcium Sensitizer," *Cardiovascular Drug Reviews* (1996) 14(3):286-316 ("Pagel"). Office Action at page 3. Applicants respectfully disagree and traverse this rejection.

The Office bears the burden of establishing a *prima facie* case of obviousness based on the prior art. *In re Fritch*, 23 U.S.P.Q.2d 1780, 1783 (Fed. Cir. 1992). The law makes it clear that obviousness must be viewed through the eyes and mind of one skilled in the art *back in time* at the moment the invention was made. *In re Dembiczak*, 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999). As noted by the Federal Circuit, strict adherence of this view avoids the temptation to simply find an invention obvious in hindsight after reading about it in the application. *Id.* In the present case, the art would not have provided any guidance to make the claimed invention, and therefore the Office has failed to establish a *prima facie* case of obviousness.

While Paralkar teaches EP_4 receptor selective agonists that "exhibit renal vasodilatory activity, and, therefore, are useful for the treatment of patients with renal impairment" (Paralkar at ¶ [0041]), Paralkar does not teach that renal vasodilators in general are effective in the treatment of renal failure.

Indeed, at the priority date of the present invention, no effective drug therapy existed for the treatment of renal failure, which is known to cause high mortality among patients. *See, e.g.,* Bonventre et al., 1st paragraph, cited by the Office in the Office Action dated January 15, 2009 at page 3. While many vasoactive agents produce renal vasodilation and increase renal blood flow in healthy subjects, such agents have failed to show benefits in subjects actually suffering from renal failure. *See, e.g.,* Bellomo et al., "Low-dose dopamine in patients with early renal dysfunction: a placebo-controlled randomised trial," *The Lancet*, 356(23/30):2139-2143 (2000) ("Bellomo").[1]

Bellomo studied a large clinical study where patients suffering from renal failure were treated by administering dopamine, a well known renal vasodilator which has been hoped to provide beneficial renal effects in healthy subjects. However, dopamine failed to improve renal parameters or survival of renal failure patients in this major clinical study. Bellomo therefore concludes that "[t]he need for effective nephroprotective agents remains." *Id.* at page 2142, right col., last paragraph. Thus, at the priority date, in view of Bellomo, a skilled artisan was aware that renal vasodilatory effect of a drug in healthy subjects does not guarantee success in the treatment of patients suffering from renal failure.

That unpredictability is further evidenced after the initial observations of Pagel, where renal effects of levosimendan were studied in animals suffering from renal failure. *See, e.g.,* Oldner et al., "Effects of levosimendan, a novel inotropic calcium-sensitizing drug, in experimental septic shock," *Crit. Care Med.*, 29(11):2185-2193 (2001)

[1] Bellomo is cited in the Information Disclosure Statement submitted herewith.

("Oldner")[2]. In Oldner, experimental septic shock (sepsis) was induced in pigs, causing, among other symptoms, acute renal failure. However, levosimendan failed to affect the endotoxin-induced reduction in renal blood flow. *See* Oldner at Abstract; page 2185, right col., first full paragraph; Figure 3 (Qrai - renal blood flow index); and page 2191, right col., first full paragraph. Accordingly, Oldner actually teaches away from the present invention, as levosimendan exhibited no beneficial renal effects in the renal failure model.

In contrast, Applicants unexpectedly found that in clinical studies with patients suffering from renal failure, levosimendan was able to reduce mortality caused by the deterioration of kidney function. Therefore, the present invention provides a significant advantage in the treatment of renal failure, a condition which was known to cause high mortality among patients and which is associated with a long-felt need for improvement.

The Office's position relies on Applicants' own teachings regarding the advantages of the claimed treatment of renal failure. That use of hindsight based on Applicants' own disclosure, however, is not permitted in an obviousness inquiry. *See In re Fritch*, 23 U.S.P.Q.2d at 1784 ("Here, the Examiner relied upon hindsight to arrive at the determination of obviousness. It is impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art so that the claimed invention is rendered obvious."). In summary, the art simply does not support a conclusion of obviousness and the rejection should be withdrawn.

---

[2] Oldner is also cited in the Information Disclosure Statement submitted herewith.

III. Conclusion

In view of the foregoing remarks, Applicants respectfully request reconsideration of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: November 18, 2009

By: Kimberly D. Smith
Kimberly D. Smith
Reg. No. 63,219
(202) 408-4000